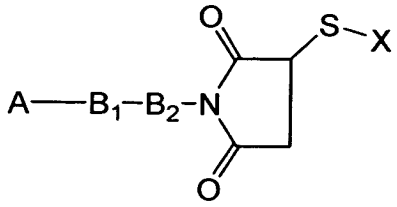
CLAIM AMENDMENTS

1.-62. (Canceled)

63. (Currently Amended) A water-soluble compound of the formula



wherein:

A is a water-insoluble drug selected from the group consisting of ~~a macrolide and an ansamacrolide~~ geldanamycin or a derivative thereof;

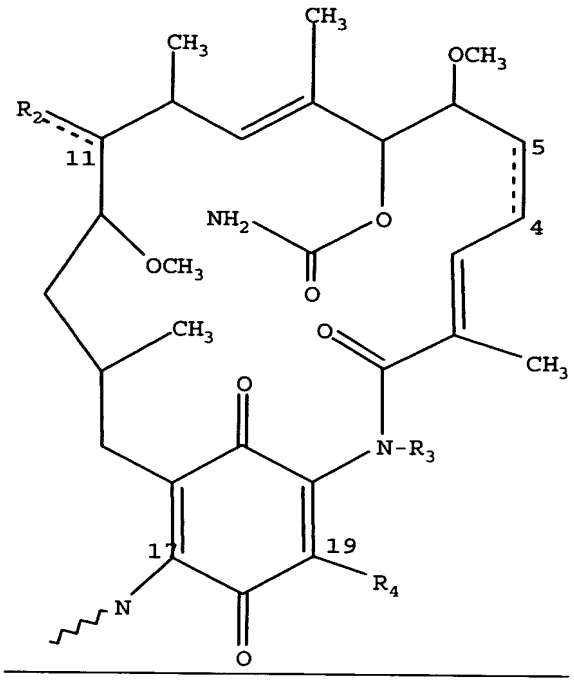
B_1 and B_2 together are a spacer moiety,

wherein B_1 is selected from the group consisting of a methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

B_2 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substitutents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group; and

X is a polar moiety selected from the group consisting of an amino acid residue, a peptide residue, a polypeptide residue, and a protein residue;

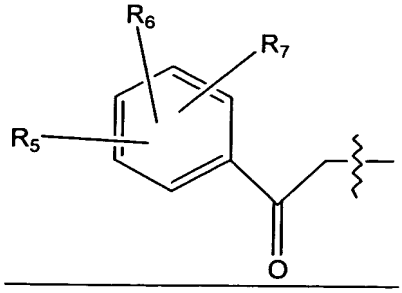
wherein the geldanamycin derivative is a compound of the formula



wherein R_2 is a halo or $-OR_8$ when there is a single bond between R_2 and the carbon at position 11, wherein R_8 is selected from the group consisting of hydrogen, a C_1-C_8 alkylamido, a C_1-C_8 alkyl, a C_2-C_8 alkenyl, a C_2-C_8 alkynyl, a C_1-C_8 hydroxyalkyl, a C_1-C_8 alkyl carbamoyl, a C_1-C_8 alkylcarbonyl, and an aralkyl, any of the R_8 groups can be substituted with one or more substituents, which can be the same or different, selected from the group consisting of nitro, a halo, azido, hydroxy, an amido, and an amino group, or

R_2 is oxo (=O) or oximino (=NOH) when there is a double bond between R_2 and the carbon at position 11,

R_3 is selected from the group consisting of hydrogen and a group of the formula



wherein R_5, R_6, and R_7 are each independently selected from the group consisting of hydrogen, a halo, an azido, a nitro, a C_1-C_8 alkyl, a C_1-C_8 alkoxy, an aryl, a cyano, and an $NR_{10}R_{11}R_{12}$, wherein R_{10}, R_{11}, and R_{12} are each independently selected from the group consisting of hydrogen and a C_1-C_3 alkyl,

R_4 is selected from the group consisting of hydrogen, a halo, a C_1-C_8 alkylamino, and a C_1-C_8 dialkylamino, and

the bond between the carbons at positions 4 and 5 can be a single bond or a double bond,

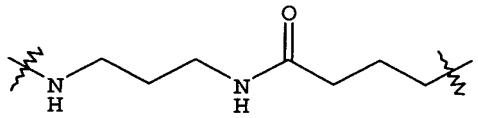
or a pharmaceutically acceptable salt of said compound.

64. (Canceled)

65. (Previously Presented) The compound of claim 63, wherein

B_2 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7 alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more residues, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino group.

66. (Previously presented) The compound of claim 65, wherein said spacer moiety has the structure



67. (Canceled)

68. (Previously presented) The compound of claim 63, wherein said polar moiety is L-cysteinyl.

69. (Previously presented) The compound of claim 63, wherein said polar moiety is ionic at neutral pH.

70. (Previously presented) The compound of claim 69, wherein said compound is zwitterionic at neutral pH.

71. (Canceled)

72. (Currently amended) The compound of claim 63, wherein said drug is geldanamycin ~~or a derivative thereof~~.

73. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 63.

74. (Canceled)

75. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 65.

76. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 66.

77. (Previously presented) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 63, whereupon the cancer in the mammal is treated, wherein the cancer expresses heat shock protein 90 (Hsp90).

78. (Canceled)

79. (Previously presented) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 65, whereupon the cancer in the mammal is treated, wherein the cancer expresses Hsp90.

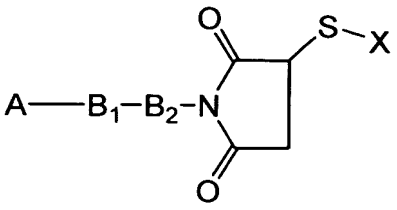
80. (Previously presented) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 66, whereupon the cancer in the mammal is treated, wherein the cancer expresses Hsp90.

81. (Currently amended) A method of rendering soluble in water a water-insoluble drug, which method comprises:

(i) providing a water-insoluble drug comprising a side-chain that can react with a bifunctional linking molecule;

(ii) contacting said water-insoluble drug with said bifunctional linking molecule to obtain a first derivative comprising a maleimide side-chain; and

(iii) contacting said first derivative with a thio containing polar moiety (X-SH) to obtain a water-soluble compound of the formula



wherein:

A is a water-insoluble drug selected from the group consisting of ~~a macrolide and an ansamacrolide~~ geldanamycin or a derivative thereof;

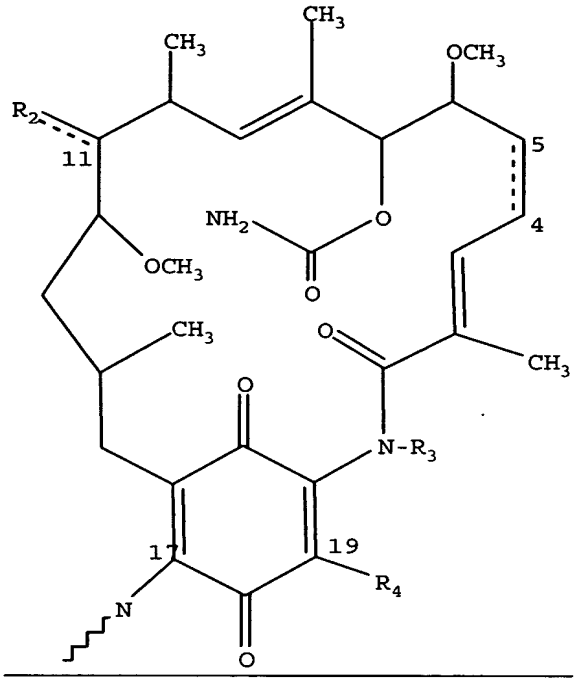
B_1 and B_2 together are a spacer moiety,

wherein B_1 is selected from the group consisting of methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

B_2 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more residues, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino group; and

X is a polar moiety selected from the group consisting of an amino acid residue, a peptide residue, a polypeptide residue, and a protein residue;

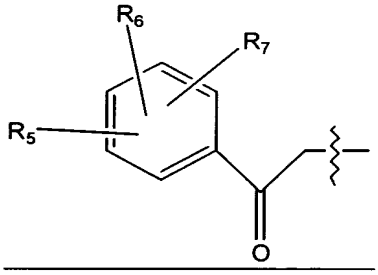
wherein the geldanamycin derivative is a compound of the formula



wherein R_2 is a halo or $-OR_8$ when there is a single bond between R_2 and the carbon at position 11, wherein R_8 is selected from the group consisting of hydrogen, a C_1-C_8 alkylamido, a C_1-C_8 alkyl, a C_2-C_8 alkenyl, a C_2-C_8 alkynyl, a C_1-C_8 hydroxyalkyl, a C_1-C_8 alkyl carbamoyl, a C_1-C_8 alkylcarbonyl, and an aralkyl, any of the R_8 groups can be substituted with one or more substituents, which can be the same or different, selected from the group consisting of nitro, a halo, azido, hydroxy, an amido, and an amino group, or

R_2 is oxo (=O) or oximino (=NOH) when there is a double bond between R_2 and the carbon at position 11,

R_3 is selected from the group consisting of hydrogen and a group of the formula



wherein R_5, R_6, and R_7 are each independently selected from the group consisting of hydrogen, a halo, an azido, a nitro, a C_1-C_8 alkyl, a C_1-C_8 alkoxy, an aryl, a cyano, and an $NR_{10}R_{11}R_{12}$, wherein R_{10} ,R_{11}, and R_{12} are each independently selected from the group consisting of hydrogen and a C_1-C_3 alkyl,

R_4 is selected from the group consisting of hydrogen, a halo, a C_1-C_8 alkylamino, and a C_1-C_8 dialkylamino, and

the bond between the carbons at positions 4 and 5 can be a single bond or a double bond,

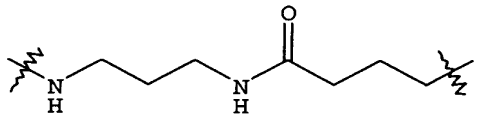
or a pharmaceutically acceptable salt of said compound.

82. (Canceled)

83. (Previously presented) The method of claim 81, wherein

B_2 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7 alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more residues, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group.

84. (Previously presented) The method of claim 83, wherein said spacer moiety has the structure



85. (Previously presented) The method of claim 81, wherein step (i) comprises contacting a water-insoluble drug with a modifying agent to provide a water-insoluble drug comprising a side-chain that can react with a bifunctional linking molecule.

86. (Previously presented) The method of claim 85, wherein said water-insoluble drug comprises a methoxyaryl moiety that can react with said modifying agent, and said modifying agent comprises a primary amine, whereupon reacting said water-insoluble drug with said modifying agent, a demethoxy derivative of said water-insoluble drug comprising a portion of said modifying agent as a side chain is provided and wherein said portion of said modifying agent can react with said bifunctional linking molecule.

87. (Previously presented) The method of claim 85, wherein said modifying agent is a diaminoalkane.

88. (Canceled)

89. (Canceled)

90. (Currently amended) The method of claim 81, wherein said water-insoluble drug is geldanamycin ~~or a derivative of geldanamycin~~.

91. (Previously presented) The method of claim 81, wherein said bifunctional linking molecule is selected from the group consisting of N-γ-maleimidobutyryloxysuccinimide ester (GMBS), sulfo-N-γ-maleimidobutyryloxysuccinimide ester (sulfo-GMBS), *m*-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS), *m*-maleimidobenzoyl-N-hydroxysulfosuccinimide ester (sulfo-MBS), succinimidyl4-[*p*-maleimidophenyl]butyrate (SMPB), sulfosuccinimidyl4-[*p*-maleimidophenyl]butyrate (sulfo-SMPB), succinimidyl 4-[N-maleimidomethyl]cyclohexane-1-carboxylate (SMCC), sulfosuccinimidyl 4-[N-maleimidomethyl]cyclohexane-1-carboxylate (sulfo-SMCC), 4-[N-maleimidomethyl]-cyclohexane-1-carboxylhydrazide-HCl (M2C2H), and 4-[4-maleimidophenyl]-butyric acid hydrazide-HCl (MPBH).

92.-106. (Canceled)

107. (New) The method of claim 77, wherein the cancer is selected from the group consisting of endometrial carcinoma, breast cancer, leukemia, gastrointestinal cancer, a central nervous system tumor, and tongue carcinoma.

108. (New) The method of claim 79, wherein the cancer is selected from the group consisting of endometrial carcinoma, breast cancer, leukemia, gastrointestinal cancer, a central nervous system tumor, and tongue carcinoma.

109. (New) The method of claim 80, wherein the cancer is selected from the group consisting of endometrial carcinoma, breast cancer, leukemia, gastrointestinal cancer, a central nervous system tumor, and tongue carcinoma.

110. (New) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of

claim 63, whereupon the cancer in the mammal is treated, and wherein the cancer is gastric carcinoma or adult T-cell leukemia.

111. (New) The method of claim 110, wherein the cancer is gastric carcinoma.

112. (New) The method of claim 110, wherein the cancer is adult T-cell leukemia.

113. (New) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 65, whereupon the cancer in the mammal is treated, and wherein the cancer is gastric carcinoma or adult T-cell leukemia.

114. (New) The method of claim 113, wherein the cancer is gastric carcinoma.

115. (New) The method of claim 113, wherein the cancer is adult T-cell leukemia.

116. (New) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 66, whereupon the cancer in the mammal is treated, and wherein the cancer is gastric carcinoma or adult T-cell leukemia.

117. (New) The method of claim 116, wherein the cancer is gastric carcinoma.

118. (New) The method of claim 116, wherein the cancer is adult T-cell leukemia.

119. (New) A method of inhibiting Hsp90 in a cell, which method comprises administering to the cell an inhibiting effective amount of a compound of claim 63, whereupon the Hsp90 in the cell is inhibited.

120. (New) The method of claim 119, wherein the cell is in a host.

121. (New) The method of claim 120, wherein the host is a mammal.

122. (New) A method of inhibiting Hsp90 in a cell, which method comprises administering to the cell an inhibiting effective amount of a compound of claim 65, whereupon the Hsp90 in the cell is inhibited.

123. (New) The method of claim 122 wherein the cell is in a host.

124. (New) The method of claim 123, wherein the host is a mammal.

125. (New) A method of inhibiting Hsp90 in a cell, which method comprises administering to the cell an inhibiting effective amount of a compound of claim 66, whereupon the Hsp90 in the cell is inhibited.

126. (New) The method of claim 125, wherein the cell is in a host.

127. (New) The method of claim 126, wherein the host is a mammal.

128. (New) The compound of claim 63, wherein said drug is a derivative of geldanamycin.

129. (New) The method of claim 81, wherein said water-insoluble drug is a derivative of geldanamycin.